To Be Assigned

Case No.: Page T1637P

## **AMENDMENTS TO THE CLAIMS**

Please cancel Claims 1-9 without prejudice and insert therefore new Claims 10-28. This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

Claims 1-9 (canceled)

10. (new) A compound of formula (I):

$$A^{1} - L$$

$$R^{1}$$

$$(I)$$

wherein:

A<sup>1</sup> is phenyl, a six-membered aromatic heterocycle containing one, two or three nitrogen atoms, or a five-membered aromatic heterocycle containing up to four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;

A<sup>1</sup> is unsubstituted or substituted by one, two or three substituents independently chosen from halogen, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, haloC<sub>1-6</sub>alkoxy, hydroxy, cyano, nitro and amino;

A<sup>2</sup> is phenyl, a six-membered aromatic heterocycle containing one, two or three nitrogen atoms, or a five-membered aromatic heterocycle containing up to four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;

 $A^2$  is unsubstituted or substituted by one, two or three groups independently chosen from halogen, cyano, nitro, amino,  $C_{1-6}$ alkylamino, di( $C_{1-6}$ alkyl)amino,  $C_{1-6}$ alkyl  $C_{2-6}$ alkenyl,  $C_{2-6}$ alkynyl, halo $C_{1-6}$ alkyl, hydroxy,  $C_{1-6}$ alkyl, thiol, SF<sub>5</sub>, phenyl $C_{1-6}$ alkyl and phenyl;

L is a bond or C<sub>1-6</sub>alkylene;

R<sup>1</sup> and R<sup>2</sup> independently chosen from hydrogen and C<sub>1-6</sub>alkyl;

Case No.: Page To Be Assigned T1637P

or R<sup>1</sup> and R<sup>2</sup> may, together, form a methylene or ethylene bridge;

W is halogen, C<sub>1-6</sub>alkyl, haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy or haloC<sub>1-6</sub>alkoxy;

X is O, S or NR<sup>3</sup> where R<sup>3</sup> is hydrogen, hydroxy, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkyl, cyano, C<sub>3-6</sub>cycloalkyl, a six-membered saturated heterocycle containing one or two heteroatoms independently chosen from O, N and S, and R<sup>3</sup> is, if possible, optionally substituted by C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, haloC<sub>1-6</sub>alkyl, haloC<sub>1-6</sub>alkoxy, halogen, amino, nitro, hydroxy, phenyl, a six-membered aromatic heterocycle containing up to three nitrogen atoms or a five-membered aromatic heterocycle containing up to four heteroatoms chosen from O, N and S, at most one heteroatom being O or S;

or X, together with the atom to which it is attached, and Y, form an unsaturated five-membered ring together with A<sup>2</sup>;

Y is a bond, C<sub>1-4</sub>alkylene, NH or NH(CH<sub>2</sub>)<sub>1-3</sub>; or a pharmaceutically acceptable salt thereof.

## 11. (new) A compound selected from:

- 4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
- 4-fluoro-4(pyridin-2-yl)*N*-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
- 4-fluoro-4(pyridine-2-yl)N-[4-trifluoromethylbenzyl]piperidine-1-carboxamide;
- 2-{4-fluoro-1-[4-trifluoromethylbenzoyl]piperidin-4-yl}pyridine;
- 2-(4-fluoro-1-{[4-trifluoromethylphenyl]acetyl}piperidin-4-yl)pyridine;
- 2-(4-fluoro-1-{3-[4-trifluoromethylphenyl]propanoyl}piperidin-4-yl)pyridine
- 4-fluoro-4-(1-methyl-1H-imidazol-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
- 4-methoxy-4-pyridin-2-yl-*N*-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
- 4-methoxy-4-pyridin-2-yl-N-[4-trifluoromethylbenzyl]piperidine-1-carboxamide;
- 4-fluoro-N-(4-isopropylphenyl)-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
- 4-fluoro-4-(3-methylpyridin-2-yl)-N-{4-[1,2,2,2-tetrafluoro-1-trifluoromethylethyl] phenyl}piperidine-1-carboxamide;
- N-(4-Tert-butylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
- 4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-(pentafluoro- $\lambda^6$ -sulfanyl)phenyl]piperidine-1-carboxamide;
- N-(4-Butylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
- N-(4-Benzylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;

To Be Assigned T1637P

Case No.: Page

```
N-biphenyl-4-yl-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
4-fluoro-4-(3-methylpyridin-2-yl)-N-[5-trifluoromethylpyridin-2-yl]piperidine-1-carboxamide;
4-(3-chloropyridin-2-yl)-4-fluoro-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide
4-fluoro-4-(3-fluoropyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
4-fluoro-4-(3-methoxypyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-carbothioamide;
N-cyano-4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-1-
carboximidamide;
4-fluoro-4-(3-methylpyridin-2-yl)-N-(1-phenylpiperidin-4-yl)-N-[4-trifluoromethylphenyl]piperidine-1-
carboximidamide;
4-fluoro-4-phenyl-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
(+/-)-(syn)-4-fluoro-2-methyl-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethylphenyl]piperidine-
1-carboxamide;
4-(fluoromethyl)-4-pyridin-2-yl-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
syn- and anti-3-fluoro-3-pyridin-2-yl-N-[4-trifluoromethylphenyl]-8-azabicyclo[3.2.1]octane-8-
carboxamide & 3-fluoro-3-pyridin-2-yl-N-[4-trifluoromethylphenyl]-8-azabicyclo[3.2.1]octane-
8-carboxamide;
4-fluoro-4-pyrimidin-2-yl-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
4-fluoro-4-(3-phenylpropyl)-N-[4-trifluoromethylphenyl]piperidine-1-carboxamide;
2-[4-fluoro-4-(3-methylpyridin-2-yl)piperidin-1-yl]-6-trifluoromethyl-1H-benzimidazole;
2-(4-fluoro-4-pyridin-2-ylpiperidin-1-yl)-6-(trifluoromethyl)-1H-benzimidazole;
4-fluoro-N-[4-trifluoromethylphenyl]-4-[3-trifluoromethylpyridin-2-yl]piperidine-1-carboxamide;
4-fluoro-N-(4-methylphenyl)-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
N-(4-ethylphenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
N-(4-chlorophenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
4-fluoro-4-(3-methylpyridin-2-yl)-N-[4-trifluoromethoxyphenyl]piperidine-1-carboxamide;
N-(4-cyanophenyl)-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
N-[4-dimethylaminophenyl]-4-fluoro-4-(3-methylpyridin-2-yl)piperidine-1-carboxamide;
```

12. (new) A pharmaceutical composition comprising one or more compounds of claim 10 or 11, or pharmaceutically acceptable salts thereof in association with a pharmaceutically acceptable carrier or excipient.

and pharmaceutically acceptable salts thereof.

To Be Assigned

Case No.: Page T1637P

13. (new) A compound of claim 10 or 11, or a pharmaceutically acceptable salt thereof, for use in treatment of the human or animal body.

- 14. (new) The use of a compound of claim 10 or 11, or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity.
- 15. (new) The use of a compound of claim 10 or 11, or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for the treatment or prevention of a disease or condition in which pain and/or inflammation predominates.
  - 16. (new) The process for the preparation of a compound of claim 10, which comprises:
- (A) for compounds wherein Y is NH or NH(CH<sub>2</sub>)<sub>1-3</sub>, reacting a compound of formula (II) with a compound of formula (III):

$$\begin{array}{c|c}
R^2 \\
\hline
W & N \\
\hline
A^1 & K^1 \\
\hline
(III) & (III)
\end{array}$$

wherein  $X^{T}$  is O or S, P is H or a  $C_{1-6}$ alkoxycarbonyl group such as tert-butoxycarbonyl and  $A^{T}$ ,  $A^{2}$ , L,  $R^{1}$ ,  $R^{2}$  and W are as defined in claim 10;

(B) for compounds wherein Y is a bond or C<sub>1-4</sub>alkylene, reacting a compound of formula (II) with a compound of formula (IV):

$$H_{X^1}$$
  $X^1$   $Y^A^2$ 

To Be Assigned

Case No.: Page

T1637

wherein both X1s are O or S, Y is a bond or C1-4alkylene and A2 is as defined in claim 1; or

(C) for compounds wherein X, together with the atom to which it is attached, and Y, form an unsaturated five membered ring together with A<sup>2</sup>, reacting a compound of formula (II) with a compound of formula (V):

$$Cl$$
 $Y$ 
 $A^2$ 
 $(V)$ 

wherein X, together with the atom to which it is attached and Y, form an unsaturated five membered ring together with  $A^2$ .

17. (new) A method for the treatment or prevention of physiological disorders that may be ameliorated by modulating VR1 activity, which method comprises administration to a patient in need thereof of an effective amount of a compound of claim 10 or a composition comprising a compound of claim 10.

18. (new) A method for the treatment or prevention of a disease or condition in which pain and/or inflammation predominates, which method comprises administration to a patient in need thereof of an effective amount of a compound of claim 10, or a composition comprising a compound of claim 10.